CASE ONE

Short case number: 3_17_1
Category: Endocrine & Reproductive Systems.
Discipline: Medicine
Setting: General Practice
Topic: Primary Hypothyroidism

Case

Addison Montgomery, 45 years old, presents for the results of her blood tests. She attended the surgery a few days ago complaining of tiredness and general feeling of 'slowing down', in investigating her symptoms you requested thyroid function tests. Her results are;

TSH 12 mU/L [0.3-3.5 mU/L
Free T_4 9 pmol/L [10-25 pmol/L]
Free T_3 5.5 pmol/L [3.5 – 7.5 pmol/L]

Questions

1. In exploring Addison's medical history further what are the key questions you would ask and why?
2. What are the key features of the clinical examination and why?
3. In explaining the results to Addison, she asks you about the thyroid gland and what it does – outline and explain the normal anatomy of the thyroid gland and the biochemistry and actions of thyroid hormone.
4. Explain Addison's thyroid function test results and correlate this with the normal physiology of the hypothalamic-pituitary thyroid axis.
5. Outline the three major areas of difficulty in the interpretation of thyroid function tests where there are no obvious signs or symptoms.
6. Addison enquires as to the possible causes of her thyroid problem, summarise the underlying pathophysiology in primary hypothyroidism and briefly explain the possible causes.
7. Addison asks about the treatment plan – outline the treatment and ongoing management of primary hypothyroidism.

Suggested reading:

- Kumar P, Clark ML, editors. Kumar & Clark's Clinical Medicine. 9th edition. Edinburgh: Saunders Elsevier; 2016.
- Colledge NR, Walker BR, Ralston SH, Penman ID, editors. Davidson's Principles and Practice of Medicine. 22nd edition. Edinburgh: Churchill Livingstone; 2014.

ANSWERS

1. **In exploring Addison's medical history further what are the key questions you would ask and why?**

Clinical features depend on the duration and severity of the hypothyroidism. In the patient in whom complete thyroid failure has developed insidiously over months or years many of the clinical features listed below are likely to be present. Care must be taken to identify patients with transient hypothyroidism, in whom life-long thyroxine therapy is inappropriate (after subtotal thyroidectomy or ^{131}I treatment of Graves' disease, in the post-thyrotoxic phase of subacute thyroiditis and in post-partum thyroiditis).

SYMPTOMS (*Italics = common features, * rare)*
Weight gain
Cold intolerance
Fatigue, somnolence
Hoarseness

Constipation

Carpal tunnel syndrome
Aches and pains
Muscle stiffness
Deafness
Depression
Psychosis (myxoedemamadness)*

Dry skin
Dry hair
Alopecia

Menorrhagia
Infertility
Galactorrhoea*
Impotence*

2. What are the key features of the clinical examination and why?

SIGNS
Weight gain
Hoarse voice
Goitre

Ileus
Ascites

Bradycardia
Hypertension
Pericardial and pleural effusions

Macrocytosis
Anaemia
Iron deficiency (pre-menopausal women) Normochromic

Delayed relaxation of tendon reflexes
Cerebellar ataxia
Myotonia

Myxoedema
Purplish lips
Malar flush
Carotenaemia
Vitiligo
Erythema abigne (Granny's tartan)

Periorbital oedema/myxoedema
Loss of lateral eyebrows

A consequence of prolonged hypothyroidism is the infiltration of many body tissues by the mucopolysaccharides, hyaluronic acid and chondroitin sulphate, resulting in a low-pitched voice, poor hearing, slurred speech due to a large tongue, and compression of the median nerve at the wrist (carpal tunnel syndrome).

Infiltration of the dermis gives rise to non-pitting oedema (i.e. myxoedema) which is most marked in the skin of the hands, feet and eyelids. The resultant periorbital puffiness is often striking and, when combined with facial pallor due to vasoconstriction and anaemia, or a lemon-yellow tint to the skin due to carotenaemia, purplish lips and malar flush, the clinical diagnosis is simple.

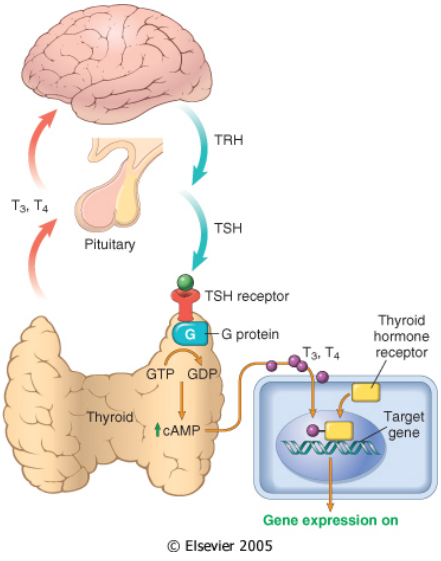
Most cases of hypothyroidism are not so obvious, however, and unless the diagnosis is positively entertained in the middle-aged woman complaining of tiredness, weight gain, depression or carpal tunnel syndrome, an opportunity for early treatment will be missed.

3. In explaining the results to Addison, she asks you about the thyroid gland and what it does – outline and explain the normal anatomy of the thyroid gland and the biochemistry and actions of thyroid hormone.

The thyroid gland consists of two bulky lateral lobes connected by a relatively thin isthmus, usually located below and anterior to the larynx.

The weight of the normal adult thyroid is approximately 15 to 25 gm. The thyroid has a rich intraglandular capillary network that is supplied by the superior and inferior thyroidal arteries. Nerve fibres from the cervical sympathetic ganglia indirectly influence thyroid secretion by acting on the blood vessels. The thyroid is divided by thin fibrous septae into lobules composed of about 20 to 40 evenly dispersed follicles. Normal follicles range from 50 to 500 µm in size, are lined by cuboidal to low columnar epithelium, and are filled with periodic acid Schiff (PAS)-positive thyroglobulin.

4. Explain Addison's thyroid function test results and correlate this with the normal physiology of the hypothalamic-pituitary thyroid axis.



Decreased levels of T_3 and T_4 stimulate the release of thyrotropin-releasing hormone (TRH) from the hypothalamus and thyroid-stimulating hormone (TSH) from the anterior pituitary

5. Outline the three major areas of difficulty in the interpretation of thyroid function tests, where there are no obvious signs or sympyoms.

One of the most common problems in medical practice is how to manage patients with abnormal thyroid function test results who have no obvious signs or symptoms of thyroid disease. For practical purposes these can be divided into three categories.

Subclinical thyrotoxicosis **-** The serum TSH is undetectable and the serum T_3 and T_4 lie in the upper parts of their respective reference ranges. This combination is most often found in older patients with multinodular goitre. These patients are at increased risk of atrial fibrillation and osteoporosis and hence the consensus view is that such patients have mild thyrotoxicosis and require therapy, usually with ^{131}I. Otherwise, annual review is essential as the conversion rate to overt thyrotoxicosis with elevated T_4 and/or T_3 concentrations is 5% each year.

Subclinical hypothyroidism **-** The serum TSH is raised and the serum T_3 and T_4 concentrations are usually in the lower part of their respective reference ranges. It may persist for many years, although there is a risk of progression to overt thyroid failure, particularly if antibodies to thyroid peroxidase are present in the serum or if the TSH rises above 10 mU/l.

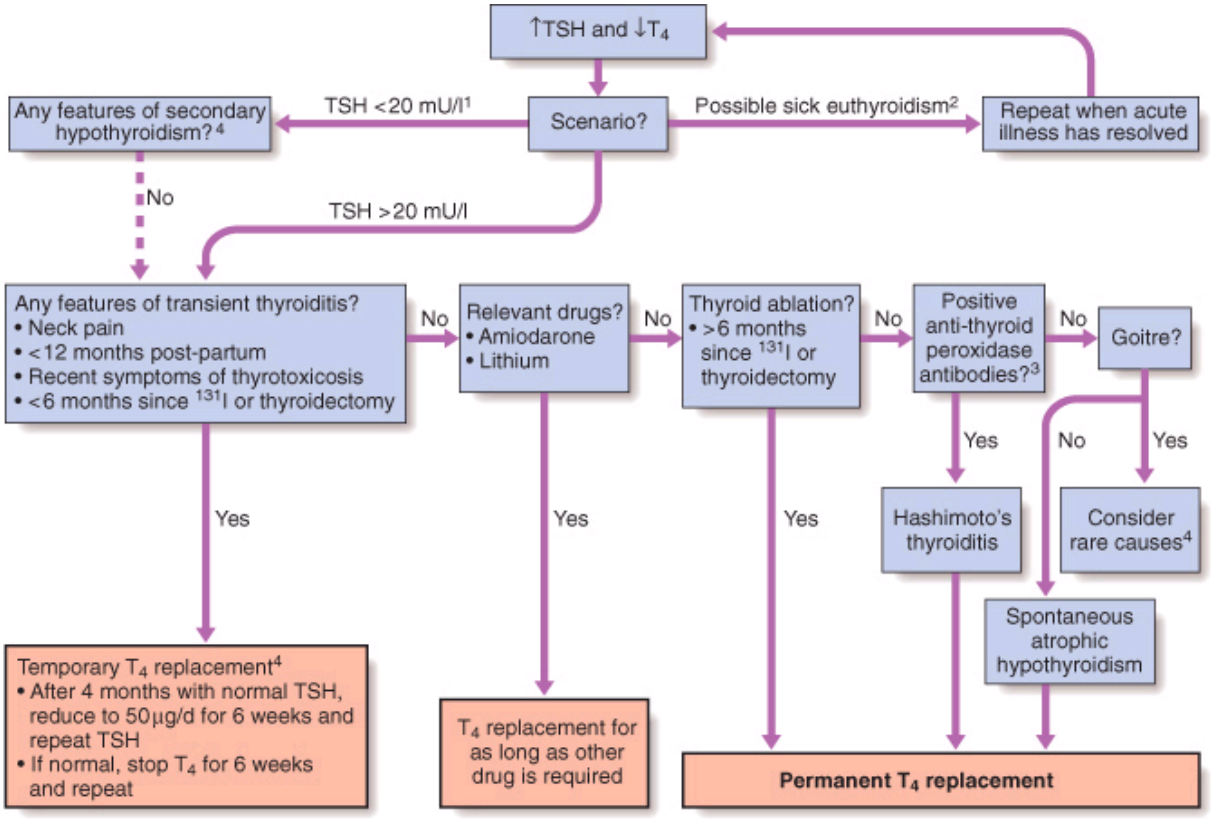
Non-thyroidal illness ('sick euthyroidism') **-** In patients with systemic illness (e.g. myocardial infarction, pneumonia) there is decreased peripheral conversion of T_4 to T_3 and alterations of

binding proteins and their affinity for thyroid hormones. In addition, serum TSH concentrations may be subnormal as a result of the illness itself or the use of drugs such as dopamine or corticosteroids. The most common combination is a low serum TSH, raised T_4 and normal or low T_3, but many patterns of thyroid function tests can be seen, dependent upon the type of assay used. During convalescence, serum TSH concentrations may increase to levels found in primary hypothyroidism. It follows that biochemical assessment of thyroid function should not be undertaken in patients with non-thyroidal illness, unless there is good evidence of concomitant thyroid disease, e.g. goitre, exophthalmos. If an abnormal result is found, treatment should only be given with specialist advice and the tests should be repeated after recovery.

6. Addison enquires as to the possible causes of her thyroid problem, summarise the underlying pathophysiology in primary hypothyroidism and briefly explain the possible causes.

CAUSES OF HYPOTHYROIDISM	Anti-PO antibodies[1]	Goitre[2]
Autoimmune		
Hashimoto's thyroiditis	++	±
Spontaneous atrophic hypothyroidism	-	-
Graves' disease with TSH receptor-blocking antibodies	+	±
Iatrogenic		
Radioactive iodine ablation	+	±
Thyroidectomy	+	-
Drugs		
Carbimazole, methimazole, propylthiouracil	+	±
Amiodarone	+	±
Lithium	-	±
Transient thyroiditis		
Subacute (de Quervain's) thyroiditis	+	±
Post-partum thyroiditis	+	±
Iodine deficiency		
e.g. In mountainous regions	-	++
Congenital		
Dyshormonogenesis	-	++
Thyroid aplasia	-	-
Infiltrative		
Amyloidosis, Riedel's thyroiditis, sarcoidosis etc.	+	++
Secondary hypothyroidism		
TSH deficiency		

7. Addison asks about the treatment plan – outline the treatment and ongoing management of primary hypothyroidism.



An approach to adults with suspected primary hypothyroidism. This scheme ignores congenital causes of hypothyroidism such as thyroid aplasia and dyshormonogenesis, which are usually diagnosed in childhood