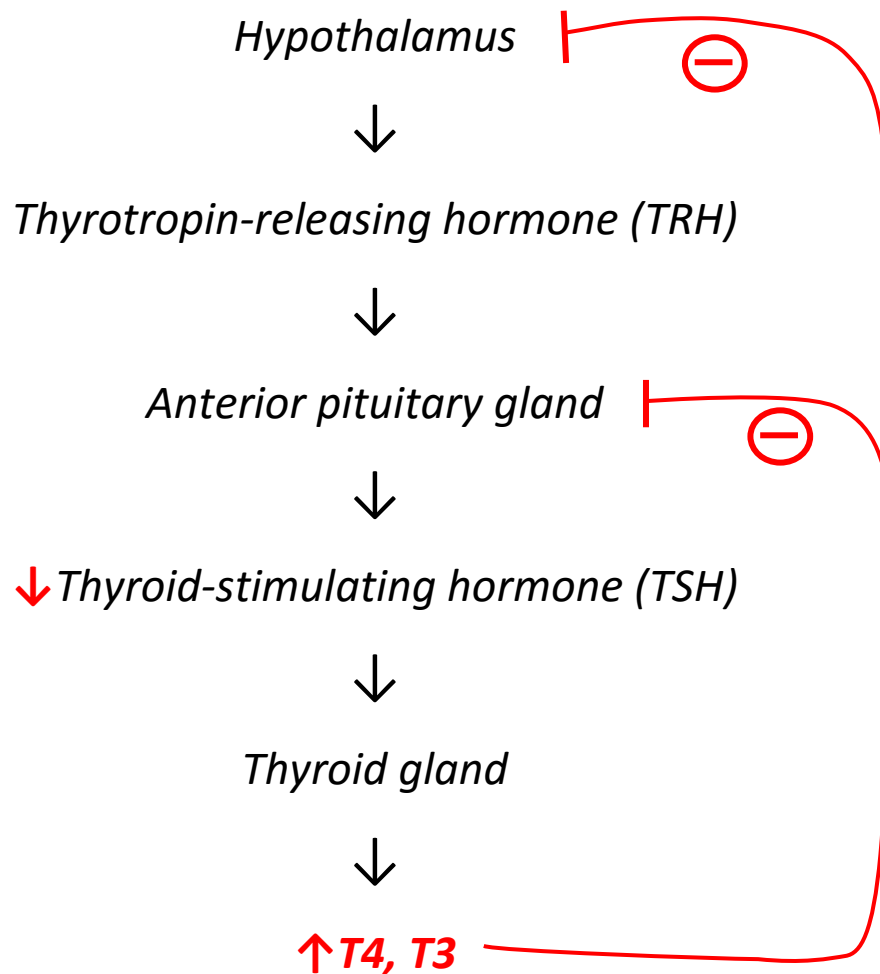


## HYPERTHYROIDISM



In hyperthyroidism, there is an increased production of thyroid hormone, in the absence of effective negative feedback. The most common cause of hyperthyroidism is Graves' disease, in which autoantibodies stimulate the TSH-receptor, even when TSH levels are low. This causes a continual stimulation of thyroid follicular cells which produce excessive amounts of thyroid hormone.

## **CAUSES**

- Grave's disease → thyroid-stimulating immunoglobulins (TSIs) bind to TSH receptor, induce Gs protein which leads to increased T3/T4 synthesis and release. Their effects on the TSH receptor last 12 x longer than TSH and lead to enlargement of the thyroid gland (goiter), hyperplasia of thyroid follicular cells, increased thyroid hormone secretion and reduced TSH production. It is more common in women aged 40-60, following a stressful event in genetically susceptible people, or following childbirth due to the increased immune response after pregnancy
- Thyroid adenoma → a localised adenoma that secretes large amounts of thyroid hormone. It is not associated with autoimmunity and causes reduced TSH production
- Toxic multinodular goiter → independently functioning nodules that produce excessive amounts of thyroid hormone. Can be caused by iodine deficiency, so is more common in less developed countries
- Thyroiditis → can be caused by infection or inflammation of the thyroid gland and may be associated with pain
- Primary hyperthyroidism can be caused by diseases of the pituitary gland and these are much more rare

## **SYMPTOMS**

### **Feeling hot**

- Increased ion channel expression via thyroid hormone → increased ion leak across membranes causes ATPases to work harder to normalise membrane potentials → generates heat
- Increase in metabolic enzyme expression causes opposing metabolic pathways to occur simultaneously → produces and synthesises ATP which produces heat
- Increase in expression of uncoupling proteins reduces thermodynamic efficiency of ATP synthesis, causing increase in heat production

### **Palpitations**

- T3 increases expression of beta receptors on myocardium → increased sensitivity to catecholamines causes increased heart rate and force of contraction (increased cardiac output)

### **Weight loss**

- Increased lipid mobilisation & fat catabolism

### **Proptosis (bulging eyes)**

- Autoantibody binds TSH receptors in retro-orbital tissue causing immune response and inflammation which can lead to fibrosis. This is often known as exophthalmos when associated with Graves' disease. In some cases this can put pressure on the optic nerve, causing damage and reduced visual acuity

### **Muscle weakness & fatigue**

- Increased protein catabolism and anabolism occurs, with a net loss of muscle
- Excess thyroid hormone causes increased CNS excitability, causing an increase in signalling across the neuromuscular junction. Thyroid hormones also reduce the expression of acetylcholinesterase, thereby reducing the breakdown of acetylcholine at the neuromuscular junction, leading to prolonged signalling to the muscles. This is known as thyrotoxic myopathy and causes muscle fibre fatigue, weakness and degradation

Owing to the effects of thyroid hormones in the body, an excess of thyroid hormone can also cause increased appetite, hyperactivity and excitability, tremor (increased sensitivity to catecholamines) and hair loss (inflammation of the hair follicles due to autoantibody mediated inflammation).

### **INVESTIGATIONS**

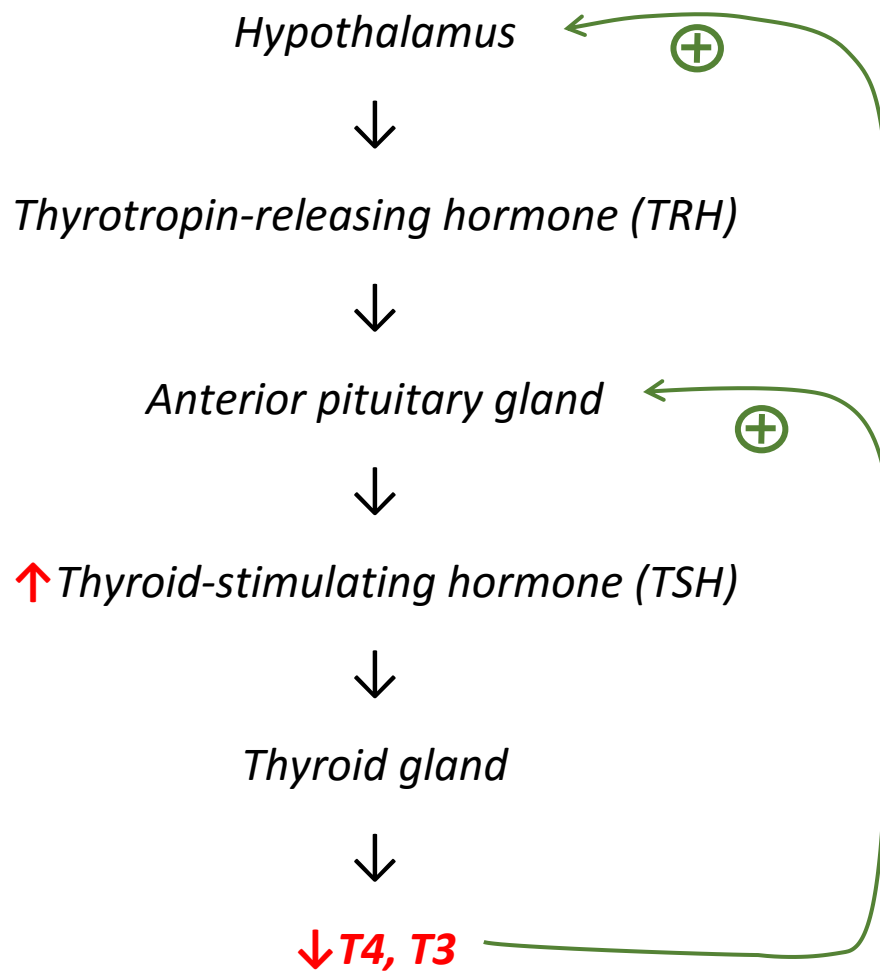
- Free T4/T3 - as these are the active hormones in the blood
- TSH - would expect this to be low due to negative feedback from high T3/T4 levels)
- Basal metabolic rate – would expect this to be high
- TSIs – high in Grave's, thyrotoxicosis, low in adenoma
- Radioactive iodine uptake tests – check whether there is a localised uptake (due to adenoma) or diffuse uptake (Grave's)

Also consider family history of autoimmune disease and examine the thyroid gland to see whether there is symmetrical enlargement of the gland or not.

### **TREATMENT & MANAGEMENT**

- **Medication**
  - Beta blockers (propranolol) – to treat tachycardia/palpitations
  - Carbimazole – reduces synthesis of thyroid hormone
- **Radioiodine therapy** – the thyroid gland is the only gland to utilise iodine. Therefore, it is the only gland to take up radioactive iodide ions and is ultimately destroyed by this. Patients may need to take levothyroxine following this treatment, a synthetic version of T4, if the function of the thyroid gland is significantly reduced as a result
- **Surgery** – to remove the affected part of the thyroid gland. There is a risk of damage to the recurrent laryngeal nerve and loss of parathyroid glands

## HYPOTHYROIDISM



Hypothyroidism often occurs when the thyroid gland is unable to produce thyroid hormones, despite high levels of stimulation by TSH. The repeated-stimulation of thyroid follicular cells causes them to hypertrophy, leading to an enlarged thyroid gland.

### **CAUSES**

- Hashimoto's thyroiditis → autoimmune disease in which autoantibodies cause inflammation and damage to the thyroid gland. Such autoantibodies may be specific to thyroid peroxidase, thyroglobulin or the TSH receptor
- Iodine deficiency → the thyroid gland is unable to produce thyroid hormone despite stimulation from TSH
- Antithyroid drugs → such as carbimazole
- Primary hypothyroidism may be caused by hypothalamic or pituitary gland disease, whereby the brain does not respond to the increased thyroid hormone levels, so reduces the production of TRH and TSH respectively. This however is rare

### **SYMPTOMS**

The symptoms of hypothyroidism are generally the opposite of those for hyperthyroidism, as they are caused by either a deficiency of, or excess of thyroid hormone which determines the level of effects of these hormones on the body.

**Tiredness/lethargy/depression** – reduced metabolic rate, reduced CNS activity

**Weight gain**

**Feeling cold**

**Hoarse voice**

**Dry skin**

**Goitre**

**Increased plasma cholesterol levels**

**Bradycardia**

**Reduced reflexes** – reduced excitability of the CNS/PNS

### **TREATMENT & MANAGEMENT**

- **Thyroid hormone replacement** - levothyroxine (synthetic form of T4)