Thyroid and parathyroid hormones and calcium homeostasis

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Abstract

The thyroid gland is under the control of thyroid-stimulating hormone (TSH) from the pituitary. It secretes thyroxine (T_4) and triiodothyronine (T_3). Iodine is essential for the synthesis of thyroid hormones. T_4 is probably converted to T_3 in peripheral tissues. Thyroid hormones have a role in growth and development, but their principal effect is the control of basal metabolic rate. Deficiency or excess affects all the tissues of the body, reducing or increasing the metabolic rate, resulting in hypothermia or hyperthermia, respectively. Deficiency during development produces mental retardation. Lack of iodine leads to thyroid swelling (goitre) caused by continuing stimulation by TSH. Calcium is one of the most tightly controlled ions in the body; abnormalities can produce muscle paralysis. Bone is the major store of calcium. Calcium reabsorption by the kidney is controlled by parathyroid hormone (PTH) produced by the parathyroid glands, which lie in the posterior part of the lobes of the thyroid gland. PTH secretion is controlled by blood calcium concentrations. Phosphate metabolism is intimately bound up with the control of calcium levels, as is the metabolism of vitamin D, which stimulates the absorption of calcium from the gastrointestinal tract and, in part, from the kidney.

Keywords Homeostasis; metabolic rate; parathyroid; thyroxine; triiodothyronine

Royal College of Anaesthetists CPD matrix: 1A01

Learning objectives

After reading this article you should be able to describe:

- the synthesis, secretion and regulation of the thyroid hormones
- the physiological effects of thyroid hormones and the consequences of over- and under-secretion
- calcium homeostasis and the role of the parathyroid gland
- the role of the kidney in calcium metabolism

The thyroid gland

The secretions of the thyroid gland affect most cells in the body. The growth and secretions of the thyroid are regulated by thyroid-stimulating hormone (TSH) secreted by the anterior pituitary, and this is controlled by thyroid-releasing hormone (TRH) from the hypothalamus.

The thyroid is one of the largest endocrine glands. It weighs about 20 g and consists of two lobes that lie either side of the trachea. The two lobes are connected by a band of tissue known as the isthmus, which lies across the front of the trachea just below the larynx. For its weight, the thyroid gland has one of the richest blood supplies of any organ or tissue in the body and a very large capacity for growth. An enlargement of the thyroid is known as a goitre and this can occur under a variety of circumstances.

Histologically, the thyroid is composed of follicles or spheres of cells (Figure 1). The cells are cuboidal in shape and the sphere is filled with a protein-rich material known as colloid. The major constituent of colloid is thyroglobulin, a large glycoprotein (i.e. protein plus carbohydrate) synthesized in the rough endoplasmic reticulum of the cells forming the follicles. The carbohydrate part of the molecule is added by the Golgi complex.

Thyroid hormones

The two thyroid hormones are thyroxine (tetraiodothyronine or T_4) and triiodothyronine (T_3). T_4 is the principal secretion; T_3 is secreted in much smaller quantities, but is more potent and in target tissues T_3 is produced from T_4.

Two other iodinated compounds, monoiodotyrosine (MIT) and diiodotyrosine (DIT), are found within the follicular cells, and small quantities are secreted into the blood. T_3 and T_4 are unique among hormones because they require a continuing supply of an inorganic constituent of the diet (iodine) for their synthesis. Mechanisms have evolved that 'trap' dietary iodine, concentrating it in the follicular cells and storing it in the thyroglobulin. Thyroglobulin, with its constituent iodine, is the precursor of T_3 and T_4. There is enough iodine in the normal thyroid to maintain T_4 production for about 2 months.

Production of these hormones involves the iodination of the amino acid tyrosine (Figure 2). Iodide (I^-) is actively taken up, by an energy-consuming process, into the thyroid follicular cells, producing an intracellular concentration 30 times higher than in the extracellular fluid. It diffuses to the apical surface of the cell, where it is oxidized to iodine and diffuses into the neighbouring colloid. Enzymes on the cell surface catalyse the iodination of tyrosine residues within the thyroglubulin molecule to form MIT and DIT (Figure 2), but still forming part of the thyroglobulin molecule. 'Coupling' of two DIT molecules in the thyroglobulin produces the precursor of T_4 and coupling of an MIT with a DIT molecule produces the precursor of T_3.

When stimulated to produce T_3 and T_4, microvilli extend from the follicular cells to engulf droplets of colloid by the process of pinocytosis. In the cell, these droplets fuse with the lysosomes where proteolytic enzymes break down the thyroglobulin to produce T_3 and T_4. These are released into the extracellular fluid on the basal surface of the cell and pass into the general circulation (Figure 1). Small amounts of MIT and DIT are also formed, but most of this is de-iodinated in the cell to produce iodide and tyrosine. Iodine is thus conserved and recycled to the colloid.

Regulation of thyroid function

Thyroid hormone synthesis and secretion are regulated by thyroid-stimulating hormone TSH (Figure 3), which comes from the anterior pituitary. TSH secretion is controlled by TRH from

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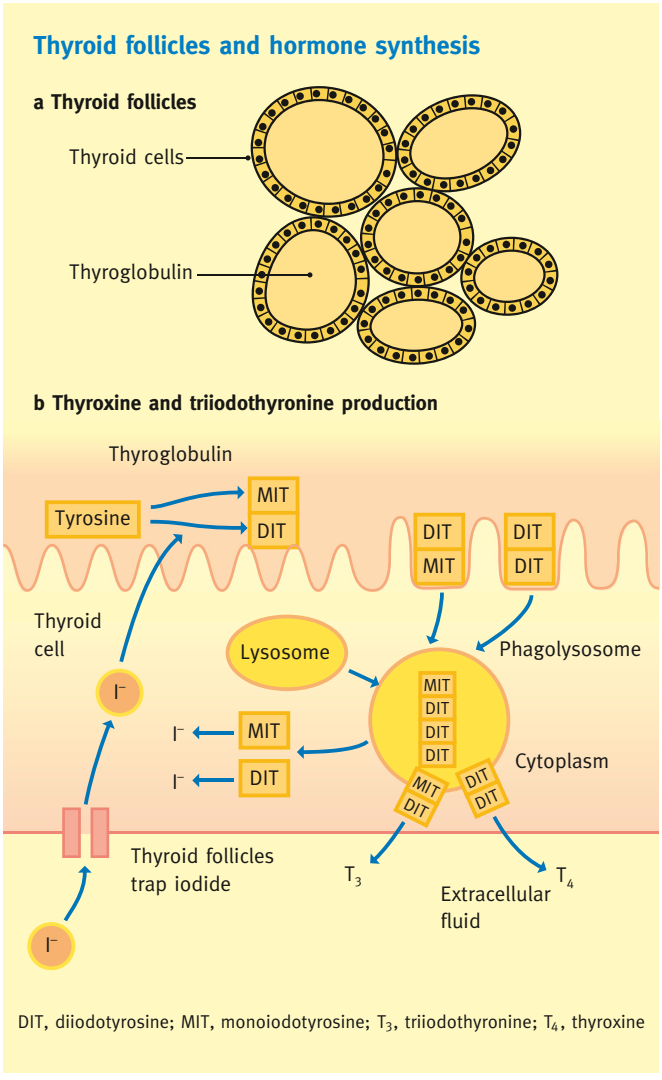

Figure 1

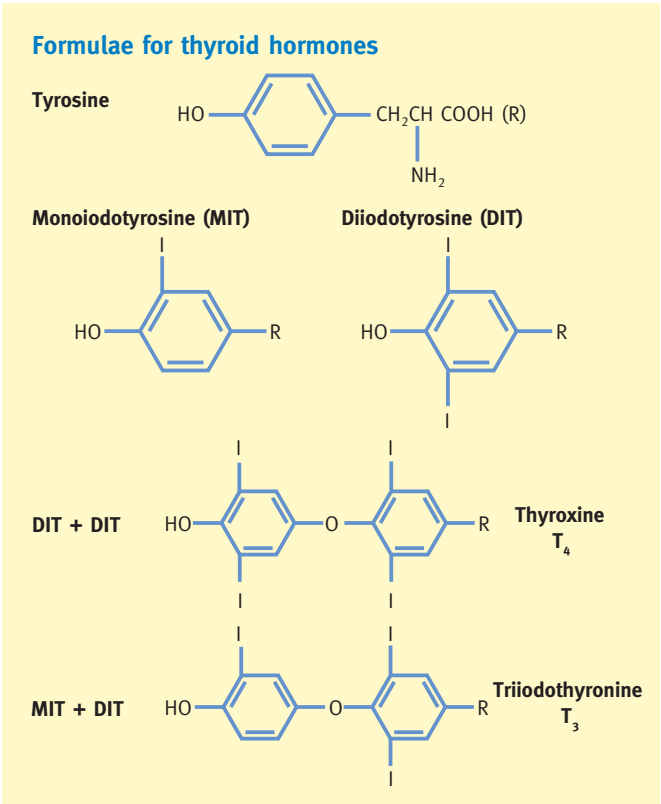

Figure 2

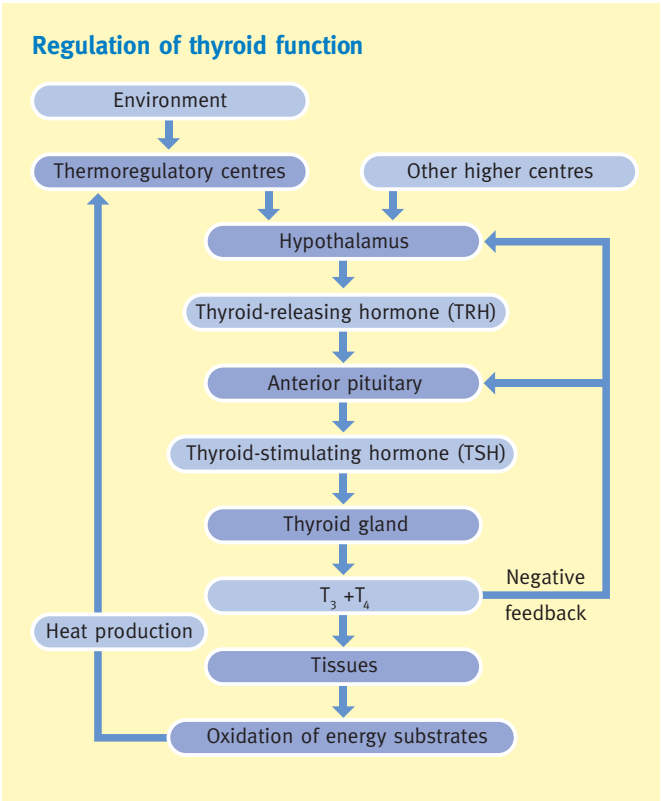

Figure 3

the hypothalamus. The hypothalamus receives inputs from higher centres including body temperature and environmental (skin) temperatures. One of the effects of both T_3 and T_4 is to increase metabolism and thereby raise body temperature. This feeds back to the hypothalamus and suppresses TRH production.

TSH is a polypeptide hormone that stimulates adenylate cyclase complex receptors on the thyroid follicular cells increasing cyclic adenosine monophosphate (cAMP). It stimulates growth of the follicular cells so they elongate and become more columnar. TSH increases all aspects of cellular activity: iodide uptake, thyroglobulin synthesis, thyroglobulin uptake by the follicular cells and the ultimate release of T_3 and T_4. Circulating concentrations of the thyroid hormones are controlled by negative feedback to the anterior pituitary (inhibiting TSH secretion) and to the hypothalamus (inhibiting TRH) (Figure 3).

Iodide can be a limiting factor to thyroid hormone synthesis. In the absence of iodide, T_3 and T_4 are not produced so do not provide the negative feedback for TSH, and the trophic effects continue unabated. The thyroid enlarges despite the inability to produce T_4, resulting in a goitre.