Thyroid, parathyroid hormones and calcium homeostasis

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Learning objectives

After reading this article you should be able to describe:

- the synthesis, secretion and regulation of thyroid hormones
- the physiological effects of thyroid hormones
- calcium and phosphate homeostasis
- the role of the parathyroid gland

Abstract

The thyroid gland secretes thyroxine (T4) and triiodothyronine (T3) in response to thyroid-stimulating hormone release from the anterior pituitary gland. Iodine is essential for the synthesis of thyroid hormones. T4 and T3 increase the basal metabolic rate, heat production, and help to maintain normal growth and development. Serum calcium levels are under very tight control. The majority of calcium is found in bones. Calcium and phosphate levels are maintained by four hormones – parathyroid hormone (PTH), calcitonin, vitamin D and fibroblast growth factor 23. PTH is produced by the parathyroid glands and its secretion is determined by serum calcium levels.

Keywords Calcium; homeostasis; parathyroid; phosphate; thyroid; thyroxine; triiodothyronine

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Thyroid

Anatomy

The thyroid is a large endocrine gland which lies anterior to the trachea, at the level of C5 to T1. It has two lobes which are connected by a central isthmus. The average weight of an adult thyroid is 20 g. It receives a rich blood supply from the superior and inferior thyroid arteries.

Microscopically, the gland is composed of spherical follicles, each of which contains a single layer of columnar cells surrounded by protein-rich colloid within the lumen. Colloid consists mainly of a large glycoprotein called thyroglobulin. Thyroid hormones are synthesized and stored within the protein of thyroglobulin.

Hormones

Hormone biosynthesis: there are two active thyroid hormones, thyroxine (T4 or tetraiodothyronine) and 3,5,3-triiodothyronine (T3). These are produced from the biologically inactive hormones, mono-iodotyrosine (MIT) and diiodothyrosine (DIT) which are found in the follicular thyroid gland in small quantities. T3 is formed when one molecule of MIT joins with one DIT; T4 is formed when two DIT molecules combine. Both T3 and T4 consist of a tyrosine molecule that is attached to a phenyl ring via an ether linkage, and have two iodine atoms on the tyrosine ring. However, T4 has two iodine atoms on its phenyl ring, whereas T3 only has one (Figure 1).

Dietary iodine is essential for production of thyroid hormones, with a recommended daily intake of 150 μg/day in adults. Foods which are rich in iodine include seafood, dairy products and some vegetables. Many countries add iodine to salt to maintain adequate levels within the population's diet.

Iodide (I^-) is actively transported into thyroid follicular cells via the sodium iodine transporter on the basolateral membrane of the cell. The iodide is then oxidized in vesicles on the apical cell membrane in a process catalysed by thyroid peroxidase. It then diffuses into the colloid and becomes covalently bound to some of the tyrosyl residues of thyroglobulin. This forms MIT and DIT. Thyroid peroxidase then catalyses the 'coupling' of these residues to form T4 from two DIT residues, and T3 from one MIT and one DIT residues.

When the thyroid is stimulated to produce T3 and T4, colloid droplets containing the thyroglobulin, are reabsorbed via pinocytosis into the follicular cells. These droplets then fuse with lysosomes and the thyroglobulin is hydrolysed to form T4 and T3. These hormones are released into the extracellular fluid and then into the circulation (Figure 2).

T4 is produced solely in the thyroid gland, at a rate of 80–100 μg/day. About 20% of T3 is produced by the thyroid gland, with a production rate of roughly 30–40 μg/day. The rest is formed by extrathyroidal deiodination of T4 in target tissues. The liver and kidney are the main sites at which this occurs, but some T3 is produced in the majority of tissues. T3 is significantly more potent than T4.

Hormone transport: T3 and T4 are relatively insoluble, therefore are carried in the blood bound to serum binding proteins (Table 1). These include thyroxine-binding globulin (TBG), albumin, lipoproteins and transthyretin (TTR).

Hormone mechanism of action: thyroid hormones enter cells through membrane transporter proteins before binding to their receptor in the nucleus. This hormone-receptor complex interacts with DNA resulting in the synthesis of new mRNA and protein. There is an increase in the number of mitochondria and metabolic rate increases.

Regulation of thyroid function

The production of thyroid hormones is regulated by a negative feedback loop (Figure 3). Low circulating levels of T4 and T3

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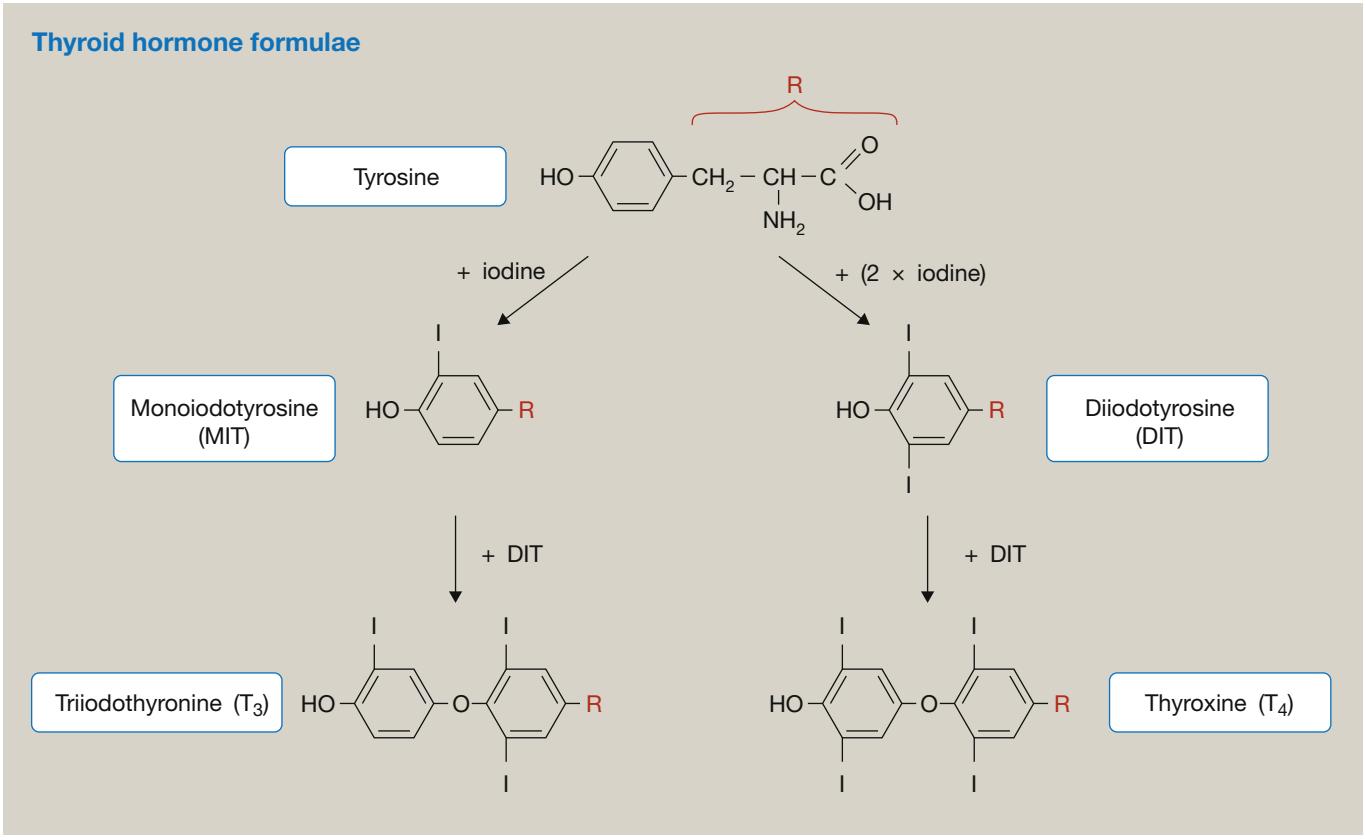

Figure 1

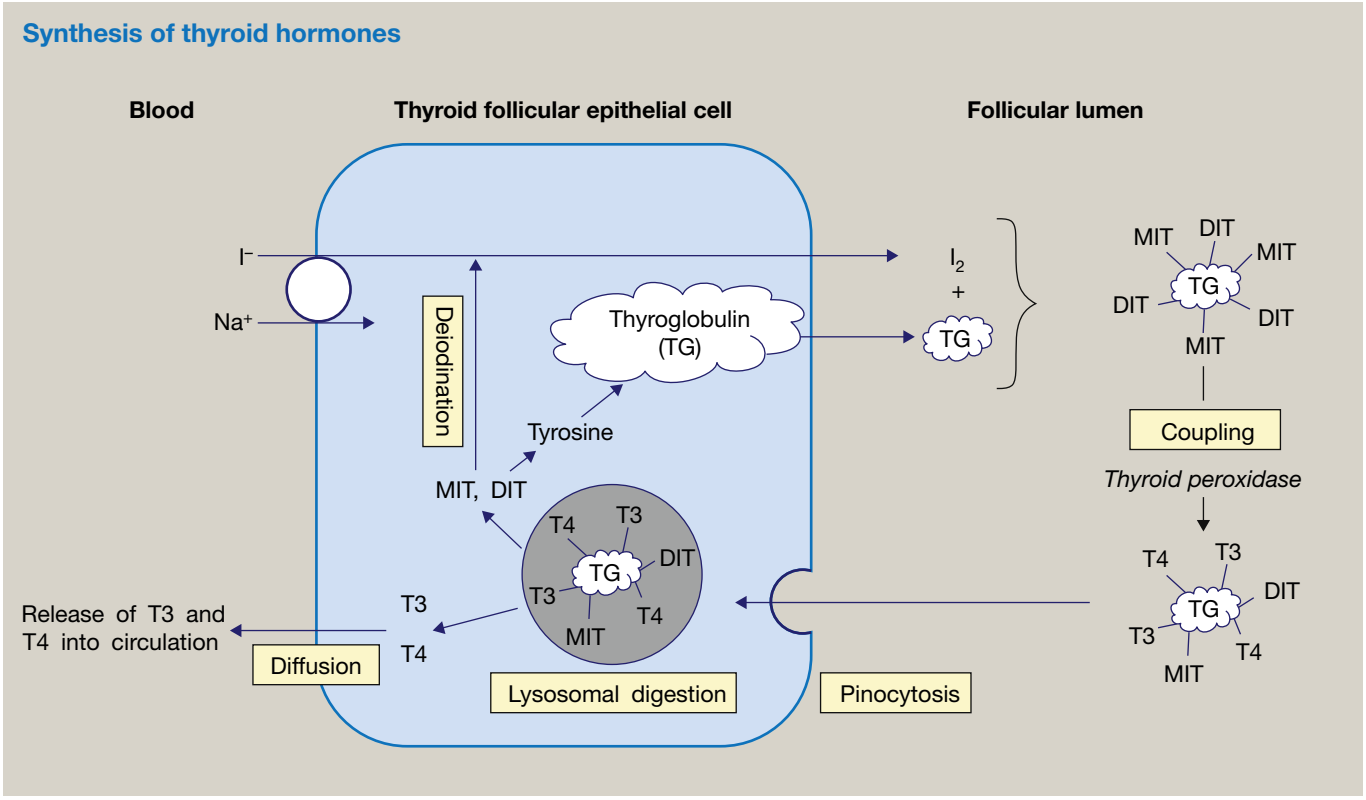

Figure 2

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