22 The Thyroid Gland. Thyroid Hormones, Their Origin and Their Mechanism of Action

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22.1 Introduction: The Endocrine System of Thyroid Hormones

Thyroid hormones (TH) are effectors of an endocrine system that influences development, growth and metabolism of practically all cells and tissues of the mammalian body. They are produced exclusively in the thyroid gland, under normal conditions mainly in the form of tetraiodothyronine (T4). The overall importance of this endocrine system is mirrored in the many physiological effects of TH on gene activation, protein synthesis and heat production (see Sects. 22.7, 22.8). It is known, for example, that normal prenatal and neonatal development of the brain in both humans and rodents depends on the presence of TH [56]. The importance of the system is also underscored by the numerous pathophysiological consequences of TH deficiency or TH excess throughout life (cf. Sect. 22.9).

The functional organization of the TH system is shown in Fig. 22.1, a schematic illustrating the production, storage and secretion of TH by the thyroid gland. TH are mainly secreted as T4, which is distributed by the circulation. In peripheral target organs TH undergo metabolic transformation in two directions:

- Activation of T4 to the physiologically most effective TH, triiodothyronine (T3); this process occurs in many tissues, mainly in liver and kidney.
- Local deactivation of T4 and T3 by further deiodination, deamination and decarboxylation [51].

The function of the thyroid gland is under regulatory control of the pituitary hormone thyrotropin (thryroid-stimulating hormone, TSH) and to a lesser degree of intrathyroidal mechanisms, cytokines and adrenergic factors.

In the present chapter we discuss:

- The functional organization of the thyroid gland
- Mechanisms that underly biosynthesis, storage and secretion of TH
- Regulation of thyroid function and growth by thyrotropin-releasing hormone (TRH), TSH and intrathyroidal factors
- Transport of TH in blood to target tissues
- Extrathyroidal metabolism of TH in target tissues
- Physiological effects of TH and, briefly, some principles of pathophysiological derangements of the thyroid endocrine system.

22.2 Functional Anatomy of the Thyroid Gland

The thyroid gland, which develops from the primitive pharyngeal epithelium, is situated on the anterior surface of the trachea. It forms two lobes, which are subdivided into irregular lobules. The position of the organ and the histological appearance of the thyroid tissue are shown in Fig. 22.2A,B. Thyroid parenchyma consists of follicles, which constitute the functional unit of the gland. They
Fig. 22.1. Functional organization of the thyroid hormone (TH) system: signal perception by the thyroid gland, hormone transport, action in target cells and inhibitory action of TH at the pituitary and hypothalamic level.

Fig. 22.2. A The position of the organ. B The macroscopic and histological appearance of the thyroid tissue. C Follicles are shown in normal (i), quiescent or hypoactive (ii), and hyperactive (iii), states. D Schematic presentation of a follicular cell showing the organelles involved in thyroglobulin (Tg) synthesis and transport into the follicular lumen. The organelles of thyrocytes are demonstrated. AM, apical membrane; BM, basal membrane; BS, blood side; C, colloid; Cap, capillaries; CC, calcitonin-producing parafollicular cells; CD, colloid droplet; CT, connective tissue; ER, cisternae of the rough endoplasmic reticulum; F, follicles; FC, follicular cells; FL, follicular lumen; G, Golgi apparatus; L, lysosome; LC, laryngeal cartilage; Lo, thyroid lobes; N, nucleus; P, pseudopod; T thyroid gland; Tr, trachea; V, exocytotic vesicles. (Reproduced, with permission, A–C from [40] and D from [22])