4.1. THYROID

4.1.1. History

Simple goiter has been recognized for centuries. In 1526, Paracelsus described goitrous cretinism. During the 1800s, several investigators described not only some of the clinical manifestations of hypothyroidal states, but surgical removal of the thyroid gland in laboratory animals led to further insight into hormone-deficient conditions. By the late 1800s, Bettancourt and Serrano reported on the relief of myxedematous symptoms in humans with the administration of sheep thyroid. Several other investigators established the usefulness of substitution therapy in the management of hypothyroidism during the latter part of the 1800s and the early 1900s. In 1896, Baumann discovered the presence of iodine in thyroid and identified diiodotyrosine. The efforts of Kendall in 1915 led to the isolation and crystallization of thyroid hormone. A decade later, Harrington and Barger actually determined the structure of thyroxin. A number of investigators, including Richter, Astwood, and McKenzie discovered chemicals that eventually became the first effective antithyroidal drugs to be used in the treatment of thyrotoxicosis or hyperthyroidism. While thyroxine was identified and characterized between 1915 and 1927, it was not until 1952 that Gross and Pitt-Rivers discovered triiodothyronine. The chemical structural requirements necessary for thyroidal activity were initially defined by Jorgensen in the 1960s, and subsequent groups of investigators, including Psychoyos and Pittman and their co-workers examined certain analogues and molecular configurations of this hormone.
4.1.2. Central Regulation of the Thyroid

The secretion of the thyroid hormones triiodothyronine (T₃) and thyroxine (T₄) from the thyroid gland is modulated by thyroid-stimulating hormone (TSH), which is secreted by the adenohypophysis (see Chapter 2 for the pharmacological use of TSH). The hormonal relationship between TSH and thyroid hormone synthesis and secretion is depicted in Figure 4-1. Hypothalamically secreted thyrotropin-releasing hormone (TRH) can enhance the secretion of TSH, in turn causing the increased synthesis and release of T₃ and T₄. The T₃ and/or T₄ released from the thyroid gland can inhibit the capacity of adenohypophyseal thyrotriph cells to respond to TRH. This property permits T₃ and/or T₄ feedback to the adenohypophysis to initiate decreased secretion of TSH; thus, these hormones regulate their own rate of synthesis and release.

A host of environmental stimuli (e.g., cold, heat, stress) can affect the hypothalamic–adenohypophyseal–thyroidal axis, resulting in changes